BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.

REMARKS

Claims 1-39 are pending in this application. Claims 34-37 are withdrawn from further consideration under 37 C.F.R. § 1.142(b). Claims 1-33, 38 and 39 stand rejected under 35 U.S.C. § 102. Claims 1 and 4 are amended. Support for the amendments can be found, for example, on pages 4-5 (paragraphs 10-11) and 29 (paragraph 139) of the as-filed specification. The specification (including Example 10) clearly indicates that the instant invention, unlike that of Chien et al., does not require inverted terminal repeat sequences from human adeno-associated virus to achieve *in vivo* cardiac-specific expression of a gene.

In addition, the specification is amended to present the abstract in a single paragraph.

No new matter is added by these amendments.

I. Formal Matters

A. The Examiner has corrected the listing of claims in Groups I and II, and decided to examine Groups I and II together based on Applicants' traversal of the restriction requirement. Office Action, at pages 2-3.

B. The Examiner alleges that the declaration is defective because "the fourth inventor has made non-initialed and/or non-dated alterations to the oath or declaration." *Id.*, at page 4. The Examiner requires a new oath or declaration in compliance with 37 C.F.R. 1.67(a).

Applicants file concurrently herewith a supplemental Declaration and Power of Attorney of coinventor Kenneth R. Chien.

II. The Claims Are Not Anticipated

A. The Examiner rejects claims 1, 2, and 4 under 35 U.S.C. § 102(a) as allegedly being anticipated by Aihara et al. (GenBank Accession Number AF131884, Database DDBJ, submitted February 15, 2000). Office Action, at page 5. The Examiner alleges that "the term 'fragment' is not defined by the claims and the specification does not provide a standard for ascertaining the requisite degree of the term 'fragment'." *Id.* Therefore, the Examiner indicates that she has given the claimed polynucleotides "their broadest reasonable interpretation." *Id.* (emphasis added). Accordingly, the Examiner states that "the limitations 'a polynucleotide comprising a fragment of SEQ ID NO:1' and 'a polynucleotide comprising a fragment of SEQ ID NO:2' have been broadly interpreted as any polynucleotide comprising at least a 2 bp fragment of SEQ ID NO:1 or any polynucleotide comprising at least a 2 bp fragment of SEQ ID NO:2." *Id.*, at pages 5-6. The Examiner asserts that Aihara et al. disclose a 2,074 bp sequence fragment of the human CVARP 5'-flanking region and, consequently, alleges that Aihara et al. anticipate claims 1, 2, and 4. *Id.*, at page 6.

Applicants respectfully traverse. According to the M.P.E.P., "[t]he identical invention must be shown in as complete detail as is contained in the . . . claim." § 2131 (quoting *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989)). In addition, the prior art reference must "clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the compound without the need for picking, choosing, and combining various disclosures...." *In re Arkley*, 455 F.2d 586, 587, 172 U.S.P.Q. 524, 526 (C.C.P.A. 1972).

The instant claims recite polynucleotides comprising fragments of SEQ ID NO: 1 and SEQ ID NO: 2. The claims also recite fragments having at least 93% and 80% sequence identity to fragments of SEQ ID NO: 1 and SEQ ID NO: 2, respectively. In contrast, Aihara et al. only disclose the identical sequence depicted in Figure 2 (i.e., SEQ ID NO: 2, which is primarily the 5'-flanking region of the human CARP gene). According to The American Heritage College Dictionary, Third Edition, a fragment is "an incomplete or isolated portion." Therefore, Aihara et al., which disclose only the entirety of SEQ ID NO: 2, do not disclose a "fragment" of either SEQ ID NO: 1 or SEQ ID NO: 2. Nor do Aihara et al. disclose a "fragment" having at least 93% sequence identity to a fragment of SEQ ID NO: 1 or 80% sequence identity to a fragment of SEQ ID NO: 2. Applicants respectfully assert that the claimed fragments are patentably distinct from the nucleic acid sequence disclosed by Aihara et al.

Moreover, Applicants contend that the Examiner's interpretation of the term "fragment" is not reasonable. The instant claims recite a polynucleotide that "specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide." Applicants respectfully assert that one skilled in the art would have no basis for concluding that a polynucleotide comprising a 2 bp fragment of SEQ ID NO:1 or SEQ ID NO:2 would be able to induce cardiac-specific expression *in vivo* of genes operably linked to the polynucleotide.

For the reasons above, Applicants request the reconsideration and withdrawal of the rejection of claims 1, 2, and 4 under 35 U.S.C. § 102(a) as anticipated by Aihara et al.

B. The Examiner rejects claims 1-7, 20-27, 30-33, 38, and 39 under 35 U.S.C. § 102(b) as allegedly being anticipated by Kuo et al. (Development, 126:4223-4234, 1999). Office Action, at page 6. According to the Examiner, Kuo et al. disclose a 10 kb fragment of the mouse CARP gene and the sequence of a 2.5 kb region upstream of the coding sequence. *Id.* The Examiner also asserts that Kuo et al. disclose 5' regulatory elements conferring cardiac-specific expression. *Id.*, at pages 6-7. Lastly, the Examiner asserts that Kuo et al. disclose transgenic mouse lines comprising a 2.5 kb sequence upstream of the CARP gene and show specific tissue and temporal expression of a transgene. *Id.*, at page 7. The Examiner again relies on a broad interpretation of the claim limitation "fragment" as a basis to allege that Kuo et al. anticipate the instant claims. *Id.*, at page 6.

Applicants respectfully traverse. As noted above, a proper prior art reference under 35 U.S.C. § 102 must disclose the identical invention and clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the compound. *See* M.P.E.P. § 2131. In addition, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Id.* (quoting *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)).

The instant claims recite a polynucleotide comprising a fragment of SEQ ID NO: 1 or SEQ ID NO: 2, wherein the polynucleotide specifically induces expression of a gene in cardiac cells *in vivo*. In addition, the claims recite an expression cassette comprising a sequence encoding a protein or RNA of therapeutic interest operably

linked to the polynucleotide. Lastly, the claims recite vectors and compositions comprising the polynucleotide or a vector and a pharmaceutically acceptable carrier.

Kuo et al. do not disclose the identical polynucleotides of the claimed invention. Instead, Kuo et al. describe the ability of portions of the 5'-flanking region of the mouse CARP gene to regulate expression of reporter genes *in vitro* in cultured cardiomyocytes versus COS1 cells. In addition, Kuo et al. only report the ability of such sequences to regulate region-specific expression of beta-galactosidase in the hearts of transgenic mice. That is, Kuo et al. fail to disclose that the CARP gene sequences only induce reporter gene expression in cardiac tissue either *in vitro* or *in vivo*. In fact, Kuo et al. report that certain portions of the 5'-flanking region of the mouse CARP gene induce reporter gene expression in skeletal muscle and forebrain. Thus, Kuo et al. do not anticipate the instant claims because they fail to disclose the identical polynucleotide fragments and do not teach every element of the claims.

For the reasons above, Applicants respectfully request the reconsideration and withdrawal of the rejection of claims 1-7, 20-27, 30-33, 38, and 39 under 35 U.S.C. § 102(b) as anticipated by Kuo et al.

C. The Examiner rejects claims 1-7, 20-25, and 28-33 under 35 U.S.C. § 102(e) as allegedly being anticipated by Chien et al. (WO 00/15821). Office Action, at page 7. According to the Examiner, Chien et al. disclose a portion 5' of the coding sequence of the mouse CARP gene that was evaluated for *in vivo* activity in adenoviral vectors. *Id.* The Examiner asserts that the levels of activity obtained were low and it was necessary to locate the promoter sequence between two inverted terminal repeats of an adeno-

associated virus in order to detect activity *in vivo*. *Id.*, at page 8. The Examiner again relies on a broad interpretation of the claim limitation "fragment" as a basis for this rejection. *Id.*, at page 7.

Applicants have amended claims 1 and 4 to recite "in the absence of inverted terminal repeat sequences from human adeno-associated virus." Applicants respectfully submit that the amendments to claims 1 and 4 obviate the Examiner's rejection because Chien et al. only describe recombinant adenovirus vector comprising a fragment of the CARP promoter in association with the inverted terminal repeat sequences from human adeno-associated virus to achieve *in vivo* cardiac-specific expression of a transgene.

Applicants request the reconsideration and withdrawal of the rejection of claims 1-7, 20-25, and 28-33 under 35 U.S.C. § 102(e) as anticipated by Chien et al.

D. The Examiner rejects claims 1-5, 8, 9, and 12-15 under 35 U.S.C. § 102(b) as allegedly being anticipated by Philip et al. (Clinical Cancer Research, 2:59-68, 1996). *Id.*, at page 8. According to the Examiner, Philip et al. disclose gene modification of primary tumor cells for active immunotherapy of cancers. *Id.* The Examiner asserts that Philip et al. disclose the design of plasmids expressing IL-2 and the transfection of such plasmids in breast cancer cells. *Id.*, at page 8. The Examiner appears to again rely primarily on a broad interpretation of the claim limitation "fragment" as a basis for this rejection. *Id.*, at page 8.

Applicants again respectfully traverse. Although claims 1-7, 20-25, and 28-33 recite that the protein or RNA of therapeutic interest is a vascular endothelial growth

factor, a fibroblast growth factor, an angiopoietin, or a cytokine (such as IL-10, IL-2, or IL-8), the claims also recite the limitation "wherein said polynucleotide specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide." Philip et al. only describe expression of IL-2 in tumor cells *in vitro*. There is no report of cardiac-specific expression of genes and there is no reason to believe that the vectors described by Philip et al. would have this property. Thus, Philip et al. do not anticipate the instant claims because they fail to disclose every element of the claims.

Applicants respectfully request the reconsideration and withdrawal of the rejection of claims 1-5, 8, 9, and 12-15 under 35 U.S.C. § 102(b) as anticipated by Philip et al.

E. The Examiner rejects claims 1-5, 10, and 11 under 35 U.S.C. § 102(b) as allegedly being anticipated by Alarco et al. (Journal of Bacteriology, 181:700-708, 1999). *Id.*, at page 9. According to the Examiner, Alarco et al. disclose the expression of the bZip transcription factor Cap1p. The Examiner again appears to rely primarily on a broad interpretation of the claim limitation "fragment" as a basis for this rejection. *Id.*

Applicants again respectfully traverse. The instant claims recite that the protein or RNA of interest is an activating or inhibiting transcription factor. The instant claims also recite the limitation "wherein said polynucleotide specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide." Alarco et al. only describe expression of the transcription factor Cap1p in yeast cells. There is no report of mammalian transcription factors or of any type of gene expression in cardiac

cells. Thus, Alarco et al. do not anticipate the instant claims because they fail to disclose every element of the claims.

Applicants respectfully request the reconsideration and withdrawal of the rejection of claims 1-5, 10, and 11 under 35 U.S.C. § 102(b) as anticipated by Alarco et al.

F. The Examiner rejects claims 1-5, 16, and 17 under 35 U.S.C. § 102(b) as allegedly being anticipated by Mohuczy et al. (Hypertension, 33:354-359, 1999). *Id.*, at page 9. According to the Examiner, Mohuczy et al. disclose the antisense expression of AT_1 receptor in vascular smooth muscle cells using an adeno-associated virus based vector. *Id.*, at page 10. The Examiner again appears to rely primarily on a broad interpretation of the claim limitation "fragment" as a basis for this rejection. *Id.*

Applicants again respectfully traverse. The instant claims recite that the RNA of therapeutic interest is an antisense RNA or a ribozyme. However, the claims also recite the limitation "wherein said polynucleotide specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide." Mohuczy et al. only describe using adeno-associated virus vector to deliver AT_1 receptor mRNA antisense with a cytomegalovirus promoter to vascular smooth muscle cells. There is no disclosure of cardiac-specific gene expression either *in vitro* or *in vivo*, and there is no reason to believe that the construct described would mediate cardiac-specific expression of, e.g., antisense RNA. Thus, Mohuczy et al. do not anticipate the instant claims because they fail to disclose every element of the claims.

Applicants respectfully request the reconsideration and withdrawal of the rejection of claims 1-5, 16, and 17 under 35 U.S.C. § 102(b) as anticipated by Mohuczy et al.

G. The Examiner rejects claims 1-5, 18, and 19 under 35 U.S.C. § 102(b) as allegedly being anticipated by Chen et al. (Circulation Research, 82:862-870, 1998). *Id.* According to the Examiner, Chen et al. disclose the overexpression of human nitric oxide synthase in rat vascular smooth muscle cells and in injured carotid artery. *Id.* The Examiner asserts that Chen et al. also disclose the design of a human endothelial nitric oxide synthase retroviral vector. *Id.* The Examiner again appears to rely primarily on a broad interpretation of the claim limitation "fragment" as a basis for this rejection. *Id.*

Applicants again respectfully traverse. The instant claims recite that the protein of therapeutic interest is nitric oxide synthase, superoxide dismutase, or catalase. However, the claims also recite the limitation "wherein said polynucleotide specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide." Chen et al. only describe expression of human nitric oxide synthase in smooth muscle cells, not cardiac cells, using a retroviral vector. There is no disclosure of cardiac-specific gene expression *in vivo*. Thus, Chen et al. do not anticipate the instant claims because they fail to disclose every element of the claims.

Applicants respectfully request the reconsideration and withdrawal of the rejection of claims 1-5, 18, and 19 under 35 U.S.C. § 102(b) as anticipated by Chen et al.

III. Response to Objection

The Examiner objects to the abstract of the disclosure because it contains three paragraphs. The Examiner alleges that the abstract should contain only a single paragraph. Office Action, at page 4.

According to the M.P.E.P., "[t]he abstract should be in narrative form and generally limited to a single paragraph within the range of 50 to 150 words." § 608.01(b) (emphasis added). However, Applicants amend the specification so that the abstract is limited to one paragraph as required by the Examiner.

IV. Conclusion

In view of the foregoing amendment and remarks, Applicants respectfully submit that the claimed invention is not anticipated by the prior art references cited by the Examiner. Applicants therefore request the reconsideration and reexamination of the application, and the timely allowance of the pending claims. Should the Examiner feel that this application is not in condition for allowance, Applicants request that she contact their undersigned representative at 202-408-4185.

Please grant any extensions of time required to enter this Amendment and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: April 6, 2004

By: 
William L. Strauss
Reg. No. 47,114

EXHIBIT 1

THE AMERICAN HERITAGE® COLLEGE DICTIONARY

THIRD EDITION

HOUGHTON MIFFLIN COMPANY
Boston • New York

Library of Congress Cataloging-in-Publication Data

The American heritage college dictionary. —3rd ed.
p. cm.
ISBN 0-395-66917-0 (plain edge). —ISBN 0-395-67161-2 (thumb edge). —ISBN 0-395-66918-9 (deluxe binding).
1. English language—Dictionaries. 2. Americanisms.
PE1628.A6227 1993
423—dc20 92-42124
CIP

Manufactured in the United States of America

For information about this and other Houghton Mifflin trade and reference books and multimedia products, visit The Bookstore at Houghton Mifflin on the World Wide Web at http://www.hmco.com/trade/.

careful handling: *fragile porcelain. Breakable* and *frangible* mean capable of being broken but do not necessarily imply inherent weakness: *breakable toys; frangible artifacts. Delicate* refers to what is so soft, tender, or fine as to be susceptible to injury: *delicate fruit. Brittle* refers to inelasticity that makes something especially likely to fracture or snap when subjected to pressure: *brittle bones.*

frag•ment (frăg′mənt) *n.* **1.** A small part broken off or detached. **2.** An incomplete or isolated portion; a bit. — *v.* (-mĕnt′) **-ment•ed, -ment•ing, -ments.** — *tr.* To break or separate (something) into fragments. — *intr.* To become broken into fragments. [ME < Lat. *fragmentum* < *frangere, frag-*, to break. See **bhreg-***.]

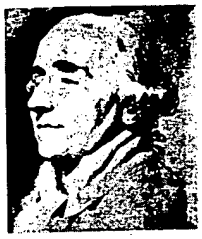
frag•men•tal (frăg-mĕn′tl) *adj.* **1.** Fragmentary. **2.** *Geol.* Consisting of broken rock, coal, or ore moved from its place of origin. — **frag•men′tal•ly** *adv.*

frag•men•tar•y (frăg′mən-tĕr′ē) *adj.* Consisting of small disconnected parts. — **frag′men•tar′i•ly** (-târ′ə-lē) *adv.* — **frag′men•tar′i•ness** *n.*

frag•men•ta•tion (frăg′mən-tā′shən, -mĕn-) *n.* **1.** The act or process of breaking into fragments. **2.** The scattering of the fragments of an exploding bomb or other projectile.

fragmentation bomb *n.* An aerial antipersonnel bomb that scatters shrapnel over a wide area upon explosion.

frag•men•tize (frăg′mən-tīz′) *tr. & intr.v.* **-tized, -tiz•ing, -tiz•es.** To fragment. — **frag′men•tiz′er** *n.*



Jean Fragonard

Fra•go•nard (frăg′ə-närʹ, frä-gô-), **Jean Honoré.** 1732–1806. French artist best known for his rococo paintings of exotic landscapes and romantic scenes.

fra•grance (frā′grəns) *n.* **1.** The state or quality of having a pleasant odor. **2.** A sweet or pleasant odor; a scent.

fra•grant (frā′grənt) *adj.* Having a pleasant odor. [ME < Lat. *frāgrāns, frāgrant-*, p.part. of *frāgrāre*, to emit an odor.]

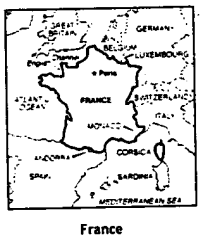
fraid•y cat (frā′dē) *n. Slang.* A timid or fearful person.

frail[1] (frāl) *adj.* **frail•er, frail•est. 1.** Physically weak; delicate. **2.** Not strong or substantial; slight: *frail evidence.* **3.** Easily broken or destroyed; fragile. **4.** Easily led astray; morally weak. [ME *frele* < OFr. < Lat. *fragilis* < *frangere, frag-*, to break. See **bhreg-***.] — **frail′ly** *adv.* — **frail′ness** *n.*

frail[2] (frāl) *n.* **1.** A rush basket for fruit, esp. dried fruit. **2.** The quantity of fruit that a frail can hold. [ME *fraiel* < OFr.]

frail•ty (frāl′tē) *n., pl.* **-ties. 1.** The condition or quality of being frail. **2.** A fault, esp. weakness of resolution, arising from the imperfections of human nature.

fraise (frāz) *n.* **1.** A defensive barrier of pointed inclined stakes or barbed wire. **2.** A ruff for the neck worn in the 16th century. [Fr. < OFr., mesentery (< its pleated shape) < *(feves) frasees*, shelled (beans) < Lat. *(faba) frēsa*, ground (bean), fem. p.part. of *frendere*, to crush. See **frenum.**]



France

frak•tur (frăk′tŏor′) *n.* A style of black letter formerly used in German manuscripts and printing. [Ger. < Lat. *fractūra*, a breaking (< the curlicues). See **fracture.**]

fram•be•sia (frăm-bē′zhə, -zhē-ə) *n.* See **yaws.** [NLat. < Fr. *framboise*, raspberry < OFr., of Gmc. orig. See **bhā-**[1]*.]

frame (frām) *v.* **framed, fram•ing, frames.** — *tr.* **1.** To build by putting together the structural parts of; construct. **2.** To conceive or design. **3.** To arrange or adjust for a purpose: *a question framed to have one answer.* **4.a.** To put into words; formulate. **b.** To form (words) silently with the lips. **5.** To enclose in or as if in a frame. **6.** *Informal.* **a.** To make up evidence or contrive events so as to incriminate (a person) falsely. **b.** To prearrange (a contest) so as to ensure a desired fraudulent outcome; fix. — *intr.* **1.** *Archaic.* To go; proceed. **2.** *Obsolete.* To manage; contrive. — *n.* **1.** Something composed of parts fitted and joined together. **2.** A structure that gives shape or support. **3.a.** An open structure or rim for encasing, holding, or bordering. **b.** A closed, often rectangular border of drawn or printed lines. **4.** A pair of eyeglasses, excluding the lenses. Often used in the plural. **5.** The structure of a human or animal body; physique. **6.** A cold frame. **7.** A general structure or system. **8.** A general state or condition. **9.** *Sports & Games.* **a.** A round or period of play in some games, such as bowling and billiards. **b.** *Baseball.* An inning. **10.** A single picture on a roll of movie film. **11.** The total area of a complete picture in television broadcasting. **12.** *Informal.* A frame-up. **13.** A single step in a sequence of programmed instruction. **14.** *Obsolete.* Shape; form. [ME *framen* < OE *framian*, to further < *fram*, forward. See **from.**]

Francis I
Portrait of Francis I, King of France by Joos van Cleve (1490?–1540?)

frame of reference *n., pl.* **frames of reference. 1.** A set of coordinate axes in terms of which position or movement may be specified or with reference to which physical laws may be mathematically stated. **2.** A set of ideas in terms of which other ideas are interpreted or assigned meaning.

fram•er (frā′mər) *n.* **1.** One that frames. **2.** Often **Framer.** One of the people who wrote the U.S. Constitution.

frame•shift (frām′shift′) *n. Genet.* The insertion or deletion in a DNA chain of a number of nucleotides not divisible by three, resulting in the incorrect reading of the codon sequence during genetic transcription.

frame-up (frām′ŭp′) *n. Informal.* **1.** A scheme to incriminate an innocent person. **2.** A contest or deliberation the outcome of which is fraudulently prearranged.

Francis Ferdinand

frame•work (frām′wûrk′) *n.* **1.** A structure for supporting or enclosing something else, esp. the skeletal support of a proposed construction. **2.** An external work platform; a scaffold. **3.** A fundamental structure, as for a written work.

fram•ing (frā′ming) *n.* A frame, framework, or system of frames.

Fra•ming•ham (frā′ming-hăm′). A town of E-central Mass. WSW of Boston; settled in 1650. Pop. 64,994.

franc (frăngk) *n.* See table at **currency.** [Fr. < OFr. < Med.Lat. *Francōrum rēx*, king of the Franks < LLat. *Francōrum*, genitive pl. of *Francus*, Frank. See **Frank.**]

France (frăns). A country of W Europe on the Atlantic and the English Channel; settled by the Franks after the retreat of the Romans. Cap. Paris. Pop. 54,334,871.

France, Anatole. Jacques Anatole François Thibault. 1844–1924. French critic and writer who won the 1921 Nobel Prize for literature.

Fran•ce•sca (frăn-chĕs′kə, frän-), **Piero della.** See **Piero della Francesca.**

Francesca da Ri•mi•ni (də rĭm′ĭ-nē, dä rē′mē-nē). d. c. 1285. Italian noblewoman who was murdered by her husband when he learned of her affair with his brother.

Franche-Com•té (frănsh-kōN-tā′). A historical region and former province of E France; first occupied by a Celtic tribe in the 4th cent. B.C. and part of France after 1676.

fran•chise (frăn′chīz′) *n.* **1.** A privilege or right officially granted a person or a group by a government, esp.: **a.** The constitutional or statutory right to vote. **b.** The establishment of a corporation's existence. **c.** The granting of certain rights and powers to a corporation. **d.** Legal immunity from servitude, certain burdens, or other restrictions. **2.a.** Authorization granted to someone to sell or distribute a company's goods or services in a certain area. **b.** A business or group of businesses established or operated under such authorization. **3.** The territory or limits within which immunity, a privilege, or a right may be exercised. **4.** *Informal.* A professional sports team. — *tr.v.* **-chised, -chis•ing, -chis•es.** To grant a franchise to. [ME *fraunchise* < OFr. *franchise* < *franche*, fem. of *franc*, free, exempt. See **frank**[1].]

fran•chis•ee (frăn′chī-zē′) *n.* One that is granted a franchise, as to market a company's goods in a certain local area.

fran•chis•er or **fran•chi•sor** (frăn′chī′zər) *n.* One that grants a franchise.

Fran•cis I (frăn′sĭs). 1494–1547. King of France (1515–47) who waged four wars against Holy Roman Emperor Charles V from 1521 to 1544.

Francis II. 1768–1835. Last Holy Roman emperor (1792–1806) and emperor of Austria (1804–35) as Francis I, who was instrumental in the defeat of Napoleon (1813–15).

Fran•cis•can (frăn-sĭs′kən) *n. Rom. Cath. Ch.* A member of a religious mendicant order founded by Saint Francis of Assisi in 1209 and now divided into three independent branches. [NLat. *Franciscānus* < Med.Lat. *Franciscus* < Saint **Francis** of Assisi.] — **Fran•cis′can** *adj.*

Francis Fer•di•nand (fûr′dn-ănd′). 1863–1914. Austrian archduke whose assassination precipitated World War I.

Francis Jo•seph I (jō′zəf, -səf, yō′zĕf) also **Franz Jo•seph I** (fränz jō′zəf, -səf, fränts, fränts yō′zĕf). 1830–1916. Emperor of Austria (1848–1916) and king of Hungary (1867–1916) whose ultimatum to Serbia led to World War I.

Francis of As•si•si (ə-sē′zē, -sē, ə-sĭs′ē), Saint. 1182?–1226. Italian Roman Catholic friar who founded the Franciscan order (1209) and was canonized in 1228.

Francis of Sales (sālz, sāl), Saint. 1567–1622. French ecclesiastic who maintained that spiritual perfection is possible for people involved in secular pursuits.

fran•ci•um (frăn′sē-əm) *n. Symbol* **Fr** An extremely unstable radioactive element of the alkali metals, having approx. 8 isotopes, the most stable of which is Fr 223 with a half-life of 21 minutes. Atomic number 87; valence 1. See table at **element.** [After **France.**]

Franck (frängk, fränk), **César Auguste.** 1822–90. French composer noted for his Symphony in D minor (1889).

Fran•co (frăng′kō, frăng′-), **Francisco.** "El Caudillo." 1892–1975. Spanish soldier and politician who directed the rebel armed forces that defeated the Republicans in the Spanish Civil War (1936–39) and ruled as dictator (1939–75).

Franco- *pref.* French: *Francophone.* [< LLat. *Francus*, Frank. See **Frank.**]

Fran•co-A•mer•i•can (frăng′kō-ə-mĕr′ĭ-kən) *n.* An American of French or French-Canadian descent. — *adj.* **1.** Of or relating to the Franco-Americans. **2.** Of or relating to France and America: *Franco-American relations.*

fran•co•lin (frăng′kə-lĭn) *n.* Any of various Eurasian or African birds of the genus *Francolinus*, related to and resembling the quails and partridges. [Fr. < Ital. *francolino.*]

Fran•co•ni•a (frăng-kō′nē-ə, -kōn′yə, frän-). A region and former duchy of S Germany. — **Fran•co′ni•an** *adj. & n.*

Fran•co•phile (frăng′kə-fīl′) also **Fran•co•phil** (-fĭl′) *n.* One who admires France, its people, or its culture. — **Fran′co•phile′** *adj.* — **Fran′co•phil′i•a** (-fĭl′ē-ə, -fēl′yə) *n.*

Fran•co•phobe (frăng′kə-fōb′) *n.* One who dislikes or fears